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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/399,083	09/17/1999	DAVID CALDERWOOD	BBIC-043/A	1842
7590 01/12/2006 GAYL B O'BRIEN ABBOTT BIORESEARCH CENTER 100 RESEARCH DRIVE WORCESTER, MA 01605-4314			EXAMINER RAO, DEEPAK R	
			ART UNIT 1624	PAPER NUMBER

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/399,083	Applicant(s) CALDERWOOD ET AL.	
	Examiner Deepak Rao	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10, 11 and 46-52 are pending in the application.
- 4a) Of the above claim(s) 11 and 48-51 are withdrawn from consideration.
- 5) ☒ Claim(s) 52 is/are allowed.
- 6) ☒ Claim(s) 1-8, 10, 46-47 are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 24, 2005 has been entered.

Claims 1-8, 11 and 46-52 are pending in this application.

Election/Restrictions

Applicant is reminded that the examination is based on the elected species (compound recited in claim 52) which reads on claims 1-8, 10, 46, 47 and 52.

Claims 11 and 48-51 are withdrawn from further consideration as being drawn to nonelected species (see MPEP §803.02) pursuant to 37 CFR 1.142(b).

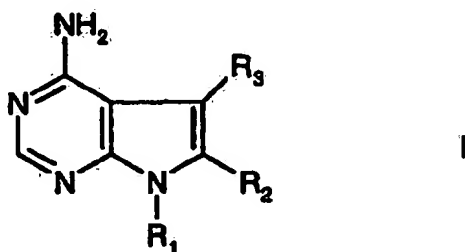
Claims 1-8, 10, 46, 47 and 52 are considered to the extent readable on the examined subgenus, i.e., structural formula of claim 1 wherein ring A is phenyl; L is -NH-SO₂-; j is 0; R₃ is substituted phenyl; R₂ is H; and R₁ is cyclopentyl, and **all** other definitions of the variables and the other species are withdrawn from consideration as being drawn to nonelected species.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Art Unit: 1624

Claims 1-8, 10, 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calderwood et al., WO 98/41525. The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I in page 2 (depicted below for convenience):



wherein R_3 is represented by formula (a)



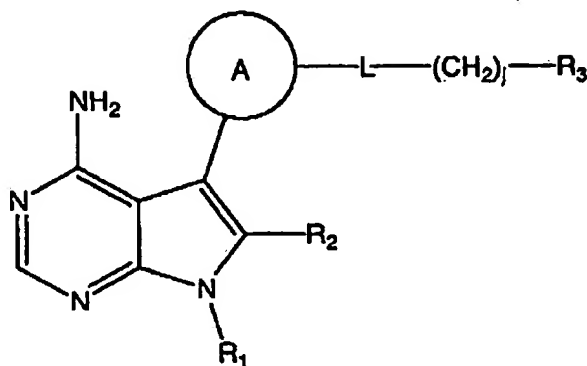
wherein the phenyl ring of formula (a) is optionally further substituted (see page 3, lines 6-9 and 25-33 and page 4 lines 1-2);

wherein the term optionally substituted phenyl means phenyl optionally substituted by one or more of the following: a) a C_{1-6} alkyl group, b) a C_{1-6} alkoxy group, c) phenoxy, d) hydroxy, e) phenyl C_{1-6} alkyl, f) halo, g) a group of formula $NR_{10}R_{11}$ in which R_{10} and R_{11} independently represent hydrogen, a C_{1-6} alkyl group, phenyl, a C_{1-6} alkanoyl group, a (C_{1-6} alkoxy)carbonyl group, 5-hydroxy-1-phenyl-3-pyrazolyl or benzoyl which is optionally substituted by C_{1-6} alkyl, C_{1-6} alkoxy or halo h) a group of formula $-COR_9$ in which R_9 represents hydroxy, a C_{1-6} alkoxy group, phenoxy or a group of formula $NR_{10}R_{11}$ in which R_{10} and R_{11} are as previously defined, i) a phthalimido group optionally substituted by halo, j) the phenyl ring is benz fused forming naphthyl or k) nitro.

A is $-NHSO_2-$ (page 3, line 10) and R_5 is optionally substituted phenyl. The reference further discloses several species that fall within the above genus, see pages 10-14, particularly page 14, lines 9-14 and 22-23. The compounds are taught to be useful as pharmaceutical therapeutic agents having protein kinase inhibition activity, see the entire document.

Art Unit: 1624

The instant claim 1 is drawn to a compound represented by structural formula:



wherein Ring A can be an optionally substituted six membered aromatic ring, e.g., optionally substituted phenyl;

L can be -NH-SO₂-;

j can be 0; and

R₃ can be an optionally substituted aromatic group, e.g., optionally substituted phenyl.

Claim 46 is drawn to specific compounds that fall within the genus of claim 1.

Applicant excluded the specific compounds disclosed in the reference by a proviso statement to overcome the anticipation rejection under 35 U.S.C. 102(a), see the amendment filed on November 30, 2004.

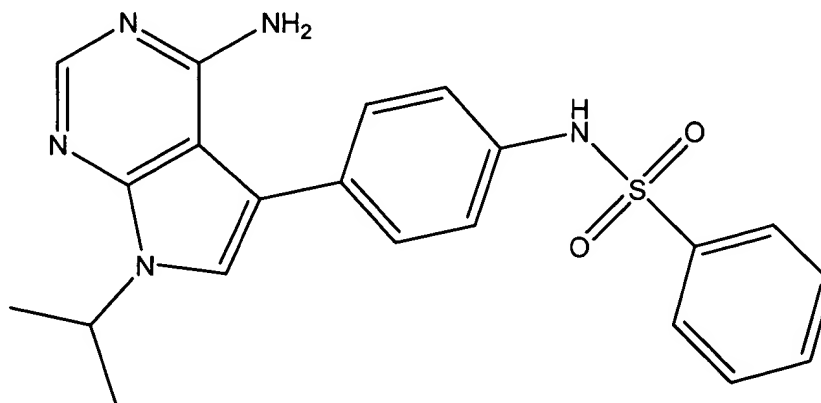
As can be seen from the description of both the reference genus and the claimed genus, it is evident that the instant claims encompass the reference genus. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as pharmaceutical

Art Unit: 1624

therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Applicant's arguments filed on October 24, 2005 have been fully considered but they were not found to be persuasive. Applicant cites MPEP § 2144.08 and argues that 'examiner has not shown that WO 98/41525 provides any suggestion or motivation to one of ordinary skill in the art to make applicant's genus as it appears in the claims'. As can be seen from the above, the instantly claimed genus encompasses the reference genus. This is further evident from the fact that applicant excluded the reference compounds from the instant claims. "When chemical compounds have 'very close' structural similarities and similar utilities, without more a prima facie case may be made", see *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

For example, the instant claims exclude the compound disclosed in page 13, lines 7-8: N-[4-(4-amino-7-isopropyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-phenyl]benzenesulphonamide (structural formula depicted below for convenience):

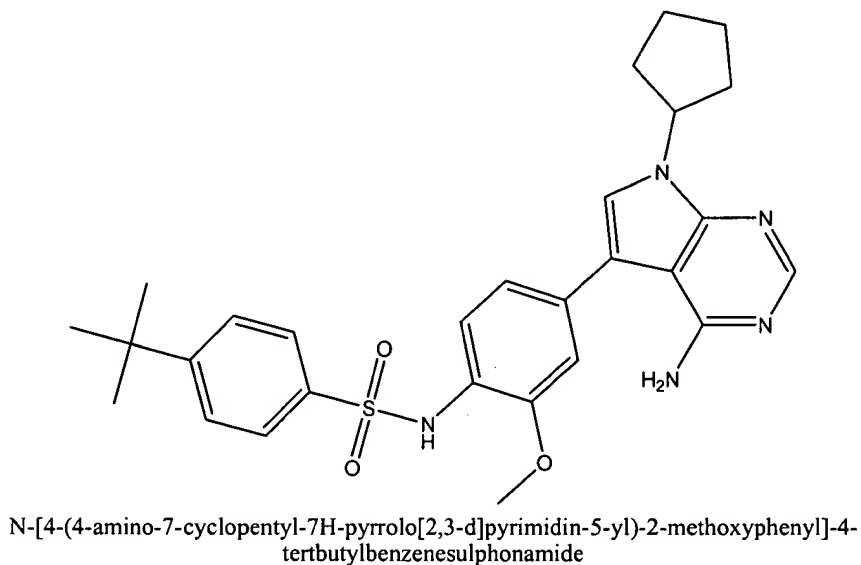


N-[4-(4-amino-7-isopropyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-phenyl]benzenesulphonamide

Art Unit: 1624

In the above species, the phenyl groups representing ring A and R₃ are unsubstituted or substituted by hydrogen. The claim, however, includes compounds wherein either of the phenyl group may be substituted by an aliphatic group, e.g., a methyl group and therefore, differ from the reference compounds by a –CH₂ group, and are therefore, structural homologs of the reference compounds.

The reference also discloses a compound, see page 14, lines 22-23 (structural formula depicted below for convenience):

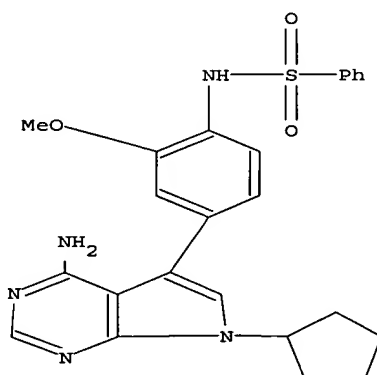


In the above species, the phenyl groups representing ring A and R₃ are substituted by a methoxy group and *tert*butyl group respectively. The above compound has been excluded from the instant claims, however, the claims include compounds wherein the methoxy is substituted on the 3-position of the phenyl; or the *t*-butyl is substituted on 2- or 3-position of the phenyl; or the phenyl is substituted by a 2-ethoxy substituent; etc. and therefore, the instant claims include structural analogs (i.e., homologs or isomers) of the reference disclosed compounds.

Art Unit: 1624

When such ‘close’ structural similarity to prior art compounds is shown, in accordance with these precedents, the burden of coming forward shifts to the applicant, and evidence affirmatively supporting unobviousness is required. *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985). Thus, it is established by case laws that a disclosed chemical compound suggests its adjacent homologs – i.e., similar compounds differing from the reference compound only by the presence or absence of a methyl substituent – and therefore, renders those homologs *prima facie* obvious.

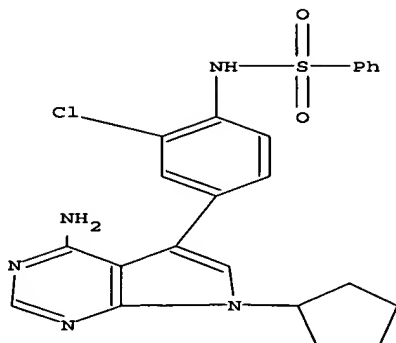
Further, the reference discloses a species which is structurally analogous to the instantly claimed compounds, see e.g., the compound of Example 34 which is depicted below for convenience:



In the above compound, the phenyl ring representing ring A is substituted by methoxy. The substituent list for ring A in the instant claims includes hydrogen, alkyl, halogen, alkoxy, etc. which is analogous with the list of substituents suggested for “an optionally substituted phenyl” in the reference.

Claim 46 of the instant application includes the species N-(4-(4-amino-7-cyclopentyl-7H-pyrrolo[2,3-d]pyrimidin-5-yl)-2-chlorophenyl)-1-benzenesulfonamide (lines 12-13) which is depicted below for convenience:

Art Unit: 1624



As can be seen from the above two structural formula, the only difference between the reference compound and the instantly claimed compound is the optional substituent at the 2-position. The reference discloses a methoxy substituent and further teaches the equivalency of alkoxy, halogen, etc. as all these are taught to be alternatives as substituents on the phenyl ring. Therefore, the reference clearly suggests the instantly claimed compounds. Further, both the reference compounds as well as the instantly claimed compounds are disclosed to be useful as tyrosine kinase inhibitors.

Applicant cites *In re Baird* and argues that ‘examiner has not established by clear and convincing evidence that one of ordinary skill in the art would have been motivated to select example 34 out of the 48 compounds disclosed in Calderwood et al. as a lead compound’. It is submitted that Example 34 was merely selected as an aid to provide the explanation for the ‘close’ structural similarities of the claimed compounds as compared to reference compounds. Example 34 is a representative compound of the reference genus that included the instantly examined subgenus based on the elected species. The reference disclosure includes several other compounds that fall within the instantly claimed genus that is withdrawn from consideration. Applicant’s arguments based on *In re Baird* are not persuasive because the decision in *Baird* was based on a big genus encompassing millions of compounds vs. a small number of claimed

Art Unit: 1624

species, “[A] disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds.” 29 USPQ2d 1552. However, the instant case involves a reference teaching genus/species vs. claimed species and not a broad genus vs. a small number of species. More specifically, as illustrated above, the reference provides a representative compound (Example 34) and further provides alternative substituents as structural variants. The instantly claimed compound is an obvious modification of the reference representative compound because in the instant compound a single substituent has been replaced by a reference suggested alternative. Therefore, motivation exists to modify the prior art compounds to prepare the instantly claimed compounds with the reasonable expectation of obtaining compounds having similar properties.

Applicant further argues that ‘in order to have a prima facie case of obviousness, there must be some suggestion or motivation in the reference to modify the reference to arrive at applicant’s genus’. However, as illustrated above, the reference provides sufficient motivation to one of ordinary skill in the art to prepare any compounds falling within the reference genus, including those that are structural analogs such as homologs, isomers, etc. “Where a claimed compound is nothing more than a homolog of a prior art compound, the prior art compound supports a prima facie case under § 103 without any particularized showing of a suggestion to modify prior art compound. See *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). “An obviousness rejection based on structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties.

Art Unit: 1624

Applicant citation of *In re Deuel* is fully considered but it not seen to be on point in the instant case. In that case, the court ruled that ‘the prior art did not disclose any relevant cDNA molecules, let alone close relatives of the specific, structurally-defined cDNA molecules of the claimed invention that might render the claims obvious’. The WO’525 reference teaches a generic group of compounds and further, expressly teaches specific compounds which fall within the genus, that formed anticipatory basis for the instant claims, which were excluded from the instant claims to overcome the rejection under 35 U.S.C. 102(a). In *Deuel* case the court clearly indicated that “a *prima facie* case of unpatentability requires that the teachings of the prior art suggest the claimed compounds to a person of ordinary skill in the art. Normally a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties. Similarly, a known compound may suggest its analogs or isomers, either geometric isomers (cis v. trans) or position isomers (e.g., ortho v. para)”, see *In re Deuel*, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995).

Applicant cites *In re Jones* to overcome the obviousness rejection. However, *Jones* dealt with the obviousness of a particular claimed ammonium salt based on a generic teaching of “substituted ammonium salts” with no Markush recitation for particular moiety, aminoethoxy ethanol, the salt on appeal. Secondary references applied in *Jones* were deemed not properly combinable with the generic disclosure in the primary reference since the references were not all

Art Unit: 1624

from the same art area. Unlike the situation in *Jones*, the instantly claimed compounds are obvious structural variants of compounds expressly taught by the reference. As explained above, the reference generically discloses all the elements of the instantly claimed genus and further, provides an example that differs only by a single substituent. Thus, the reference provides sufficient motivation for the ordinary artisan to modify the reference compounds to arrive at the instantly claimed compounds because one of ordinary skill in the art only needs to change the position of the substituent to arrive at the instant invention. Such modification would have been obvious, absent a showing of unexpected results.

The following rejections are under new grounds:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, in the list of substituents provided for Ring A includes the terms “a substituted or unsubstituted alkyl amido or **alkylcarboxamido**”; “a substituted or unsubstituted aryl amido or **arylcarboxamido**” (see page 2, last two lines); “a substituted or unsubstituted aralkyl amido, **aralkylcarboxamido**” (see page 3, lines 1-2). It is not clear what is the difference between the two alternative terms, e.g., ‘alkyl amido’ and ‘alkylcarboxamido’. The specification provides the terms ‘alkyl amido’, ‘aryl amido’ and ‘aralkyl amido’ (see pages 15-16) and the other terms

Art Unit: 1624

'alkylcarboxamido, arylcarboxamido and aralkylcarboxamido' were not found to be present in the disclosure. There is no explanation what these terms are intended to represent and where they find support in the disclosure.

Allowable Subject Matter

Claim 52 is allowed. (The reasons provided in the previous office action are incorporated here by reference).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

Art Unit: 1624

system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Deepak Rao
Primary Examiner
Art Unit 1624

January 9, 2006